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| 10/686,713 | 10/17/2003 | Michelle M. Hanna | 2072.0010006 | 9587 |

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| KIM, YOUNG J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/686,713 | HANNA, MICHELLE M. | |
| | Examiner | Art Unit | |
| | Young J. Kim | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *136-149* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *136-142 and 144-149* is/are rejected.

7)☒ Claim(s) *143* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The present Office Action is responsive to the Amendment received on September 12, 2006.

### *Preliminary Remark*

Claims 1-135 are canceled.

Claims 148-149 are new.

Claims 136-149 are pending and are under prosecution therefore.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 136, 137, 145, and 146 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on June 13, 2006 is maintained for the reasons of record.

Applicants' arguments presented in the Amendment received on September 12, 2006 have been fully noted, but they are not found persuasive for the reasons set forth in the, "Response to Arguments," section.

The Rejection:

Claim 136 is indefinite for reciting the phrase, "abortive reiterative synthesis," because the specification does not explicitly define what constitutes an abortive reiterative synthesis, so as to properly determine the metes and bounds embraced by this limitation.

Claims 137, 145, and 146 are indefinite by way of their dependency on claim 136.[1]

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[1] Claim 138, while dependent on claim 136, further defines what steps are to be conducted in an abortive RNA transcription, and thus is held definite.

Claim 146 is indefinite because the method is for detecting the presence of a target molecule, wherein the detection is achieved by detecting multiple copies of detectable oligonucleotides (i.e. nucleic acid), but claim 146 recites that the target molecule being detected is a protein.

No assumption could be made for this claim for the purpose of further prosecution on its merits.

Response to Arguments:

Applicants rely on several pages of the specification so as to define and thus justify that the claim limitation imposed by the phrase, "abortive reiterative synthesis" is definite (page 11-12, Response).

These arguments are not found persuasive because the specification does not provide an specific and explicit definition of which is considered to be involved in the process of abortive reiterative synthesis.

Applicants are reminded that MPEP 2106(II)(C) states that while it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not impose that limitation.

According to Applicants' arguments, the process of "abortive transcription" is defined as, "an enzyme-mediated process that reiteratively initiates and terminates the synthesis of oligonucleotides that correspond to at least one portion, or target site, of a complementary nucleic acid template sequence..."

Another portion of the specification states, "[a]bortive transcription also includes three phases...." (page 11, Response).

Clearly, there is not a specific definition for the process of "abortive transcription" let alone, "abortive reiterative transcription." According to the first description of the specification, such

process reads on any enzyme-mediated transcription processes. Therefore, it is maintained that it remains indefinite as to what steps are employed by the generically recited limitation, "abortive reiterative transcription."

In addition, Applicants traverse that claim 146 is not indefinite because the specification describes an embodiment in which the target molecules being detected is a protein (page 12, bottom paragraph). This is noted. However, claim 136 (which serves as the base claim for claim 146) recites that the step of "synthesizing multiple copies of detectable oligonucleotides through abortive reiterative synthesis on a nucleic acid template." Hence, it remains unclear how a protein detection is achieved based on a step of reiterative synthesis on a nucleic acid template. Applicants are invited to amend the claims to add essential steps which may be required for the claim to be definite.

The rejection is maintained therefore.

***Claim Rejections - 35 USC § 102***

The rejection of claims 136-139, 141-145, and 147 are rejected under 35 U.S.C. 102(b) as being anticipated by Daube et al. (Science, November 1992, vol. 258, pages 1320-1324), made in the Office Action mailed on June 13, 2006 is withdrawn in view of the Amendment received on September 12, 2006.

Specifically, the disclosure by Daube et al. is solely drawn to the study of RNA polymerase complex, and there is no motivation or suggestion for the use of its disclosure for a method of detecting a target molecule in a biological or environmental sample. As Applicants' correctly point out, the target nucleic acid disclosed by Daube et al. are synthetically generated solely for the purpose of studying the RNA polymerase complex (see arguments presented on page 14, bottom paragraph, Response).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 136-138, 140, and 145-147 under 35 U.S.C. 102(b) as being anticipated by Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460), made in the Office Action mailed on June 13, 2006 is maintained for the reasons of record.

***In addition,*** claims 148 and 149 are rejected herein as being necessitated by Amendment (by way of their addition).

Applicants' arguments presented in the Amendment received on September 12, 2006 have been fully noted, but they are not found persuasive for the reasons set forth in the, "Response to Arguments," section.

The Rejection:

Sasaki et al. disclose a transcriptional sequencing method, said method comprising the steps:

a) synthesizing multiple copies of detectable oligonucleotides through abortive reiterative synthesis on a nucleic acid template (accomplished by a nucleic acid template comprising a T7 promoter sequence T3 promoter sequence and RNA polymerase; see Figure 4 on page 3457, wherein the abortive reaction is achieved by incorporation of four kinds of dye-3' dNTPs);

b) detecting said oligonucleotide, thereby determining the sequence (or presence) of said target molecule (page 3457, 2nd column, Figure 4 description), thereby clearly anticipating claim 136.

With regard to claim 137, the artisans employ RNA transcription on a DNA template comprising promoter sequences (page 3455, 2nd column, bottom paragraph; page 3456, 1st column bottom paragraph through 2nd column, 1st paragraph).

With regard to claim 138, the method involves the incubation of DNA template with an initiator (primers comprising T7 promoter sequence and T3 promoter sequence), followed by the incubation with RNA polymerase (see Figure 4), followed by the detection of the synthesized multiple reiterative oligonucleotide transcripts (by sequencing).

With regard to claim 140, the transcript termination is achieved through incorporation of a nucleotide analog, dye-3' dNTPs (fluorescent dye terminators; *see* page 3457, 1st column, bottom paragraph).

With regard to claim 145, the target molecule is a nucleic acid (page 3456, 2nd column, 1st paragraph).

With regard to claim 147, the nucleic acid template comprises a structure which allows the abortive reiterative synthesis to occur. Since the specification does not have a specific definition of what is considered to by an "abortive promoter cassette," and since the claims do not recite a structure of such cassette, based on a reasonable broadest interpretation of the claim, any structure which comprises promoter sequence that is capable of effecting abortive reiterative synthesis, is deemed to meet this limitation.

Therefore, Sasaki et al. clearly anticipate the invention as claimed.

Response to Arguments:

Applicants contend that the disclosure of Sasaki et al. cannot anticipate the invention as claimed because Sasaki et al. does not disclose an "abortive reiterative synthesis reaction."

Applicants' refer to an exemplary definition found on the specification that appears to define the limitation. However, it was already maintained above that the claim term, at best, was indefinite, and that the term was broad enough to embrace other means of transcription.

MPEP 2106(II)(C) states that while it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not impose that limitation.

Applicants contend that the term, "reiterative" refers to "multiple identical or highly similar copies of a sequence of interest (page 13, bottom paragraph, Response) and state that the transcripts generated by Sasaki et al. are heterogeneous in size (page 13, bottom paragraph, Response).

While the transcription reaction disclosed by Sasaki et al. may product a plurality of transcripts may produce a heterogeneous-size population of transcripts, the term, "plurality" requires at least two transcripts at minimum. It is implausible to think that the transcription reaction generated by Sasaki et al. were not capable of producing a transcript which is terminated at the same base location. In addition, the claims do not recite that the abortive reiterative synthesis generate multiple transcripts of identical lengths. In addition, while the specification may disclose that the process may generate multiple identical or highly similar copies of a sequence of interest, the specification does not justify for transcripts which have identical length. It is also important to note that the phrase, "highly similar copies of a sequence of interest," is open to sequences which may or may not be of same length or sequence.

Applicants also contend that the fragment sizes of transcripts generated by Sasaki et al. range up to at least 600 nucleotides in length, and such heterogeneous fragments are not the products of reiterative process because they are not "identical or highly similar copies."

Firstly, Applicants' reliance on an exemplary disclosure of the process considered to be "abortive transcription" does not overcome the rejection because such limitation is not actively presented in the claims.

In addition, it is again submitted that the method of Sasaki et al. is capable of generating more than one transcript of the same length. It is implausible to think that out of all heterogeneous population of transcripts produced by Sasaki et al., at least two transcripts are not terminated at the position by the incorporation of the same chain-terminating nucleotide, thereby producing at least two transcripts of identical lengths, or even nucleotides of similar lengths.

The rejection is proper and thus maintained.

***Necessitated by Amendment***

Claims 136-139, 141, 142, 144, 145, and 147-150 are rejected under 35 U.S.C. 102(b) as being anticipated by Daube et al. (PNAS USA, September 1994, vol. 91, pages 9539-9543) as evidenced by Daube (Biochemistry, 1994, vol. 33, pages 340-347, herein "Daube-2").

Daube et al. disclose a method of detecting the presence of a target molecule from a plasmid, pAR1707 (thus a biological sample; *see* page 9540, 1st column, 2nd paragraph), wherein the artisans conduct the step of ligating a transcriptional bubble complex to the target nucleic acid (see Figure 1 on page 9540), followed by the generation of the multiple abortive reiterative transcripts (page 9540, 2nd column, 2nd paragraph), followed by their detection (page 9540, 2nd column, 2nd paragraph, detection by gel electrophoresis), thereby clearly anticipating claim 136, 144, 145, 147, 148, and 149.

With regard to claim 137, the transcription is an RNA transcription on a DNA template (page 9540, 1st column, see 180-bp DNA fragment being employed).

With regard to claims 138, 141, and 142, RNA primer is employed (thus, an initiator; see Figure 1E on page 9540), and the termination of the transcription products by the termination sequence located downstream from the initiation sequence (Figure 2 on page 9541).

With regard to claim 139, Daube et al. refers to the method disclosed by Daube-2, wherein in the disclosure of Daube-2, on page 342, the step of nucleotide-deprivation is employed (deprivation of GTP, see page 342, 2nd column, 2nd paragraph).

Therefore, the invention as claimed is anticipated by Daube et al. as evidenced by Daube-2.

### *Claim Rejections - 35 USC § 103*

The rejection of claim 140 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daube et al. (Science, November 1992, vol. 258, pages 1320-1324) in view of Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460), made in the Office Action mailed on June 13, 2006 is withdrawn in view of the Amendment received on September 12, 2006.

Specifically, the disclosure by Daube et al. is solely drawn to the study of RNA polymerase complex, and there is no motivation or suggestion for the use of its disclosure for a method of detecting a target molecule in a biological or environmental sample.

As Applicants' correctly point out, the target nucleic acid disclosed by Daube et al. are synthetically generated solely for the purpose of studying the RNA polymerase complex (see arguments presented on page 14, bottom paragraph, Response).

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 136-147 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 7,045,319, made in the Office Action mailed on June 13, 2006 is maintained for the reasons of record.

Applicants' request to hold the rejection in abeyance is noted (see page 18, 2nd paragraph, Response).

However, the instant application contains multiple substantive rejections over prior art and thus, rejection is maintained.

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the issued patents are narrower species of method which renders the broader claims of the instant application in a genus-species anticipatory way.

The provisional rejection of claims 136-147 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26, 27, 103, 112, and 136-139 of copending

Application No. 10/488,971 (herein, the '971 application), made in the Office Action mailed on June 13, 2006 is maintained for the reasons of record.

Applicants' request to hold the rejection in abeyance is noted (see page 18, 2nd paragraph, Response).

However, the instant application contains multiple substantive rejections over prior art and thus, rejection is maintained.

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of the '971 application are narrower species of method which renders the broader claims of the instant application in a genus-species anticipatory way.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The provisional rejection of claims 136-147 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22, 32-34, and 44 of copending Application No. 10/976,240 (herein, the '240 application), made in the Office Action mailed on June 13, 2006 is maintained for the reasons of record.

Applicants' request to hold the rejection in abeyance is noted (see page 18, 2nd paragraph, Response).

However, the instant application contains multiple substantive rejections over prior art and thus, rejection is maintained.

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the claims of the '240 application require the same method of reiteratively synthesizing oligonucleotide transcripts which are terminated, as well as employing an abortive promoter cassettes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The provisional rejection of claims 136-147 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-27 of copending Application No. 10/425,037, made in the Office Action mailed on June 12, 2006 is maintained for the reasons of record.

Applicants' request to hold the rejection in abeyance is noted (see page 18, 2nd paragraph, Response).

However, the instant application contains multiple substantive rejections over prior art and thus, rejection is maintained.

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of the instant application and the claims of the '240 application require the same method of reiteratively synthesizing oligonucleotide transcripts which are terminated, as well as employing an abortive promoter cassettes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The provisional rejection of claims 136-147 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over pending (and/or elected) claims of copending Application No. 10/602,045; 10/602,045; and 10/607,136, made in the Office Action mailed on June 12, 2006 is maintained for the reasons of record.

Applicants' request to hold the rejection in abeyance is noted (see page 18, 2nd paragraph, Response).

However, the instant application contains multiple substantive rejections over prior art and thus, rejection is maintained.

With regard to Applicants' request for clarification of Application no. 10/600,045, the citation contained a typographical error. The correct application no. should be 10/602,045.

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other because as reasons already set forth above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the

mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Inquiries***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be

sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Primary Examiner
Art Unit 1637
11/27/2006

YOUNG J. KIM
PRIMARY EXAMINER

YJK